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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,277	03/06/2002	Thomas Ehrhardt	50716	2896

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,277	EHRHARDT ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-8,11-13 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. ***Election***

Applicants' election with traverse of Group V [claims 9, 10 & 14], in their response filed November 29, 2004 is acknowledged. The traversal is on the grounds that 'the DNA sequence which codes for a plant dihydroorotase and use of said sequence form a single general inventive concept under PCT Rule 13.1. Therefore, the examiner's restriction requirement is improper. Applicants request its withdrawal.

Applicants' arguments have been considered by not found to be persuasive because - where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Applicants' Group II claim 3, for example, is drawn to "a protein with dihydroorotase activity and comprises an amino acid sequence which constitutes a SEQ ID NO: 2 subsequence of at least 100 amino acids" [and these 100 amino acids do not have to be contiguous] and such a sequences, a dihydroorotase from *Arabidopsis thaliana*, is disclosed in the prior art works of Zhou et al. [Plant Physiol. 114: 1569 (1997); Accession No. AF000146]. This prior art is also cited in Applicants' specification on page 2, lines 9-10. Zhou et al. also disclose the corresponding DNA [encoding dihydroorotase] which is 46.2% identical to Applicants' SEQ ID NO: 1. According to the instant specification, page 6, 3rd paragraph, Applicants' dihydroorotase from *Solanum tuberosum* [or SEQ ID NO: 2] is 78% identical to the *Arabidopsis thaliana* dihydroorotase. (see Example 2).

In the Examiner's sequence search, accession no. T05124 [23 rd April, 1999], also a dihydroorotase from *Arabidopsis thaliana* – was found to be 81% identical to Applicants' SEQ ID NO: 2, and has more than 100 matches to qualify as a prior art for the protein of Group II, claim 3 [see the enclosed sequence search alignment]. As a consequence the cited prior art defines that the technical feature so claimed as not a contribution over the cited prior art. Therefore, Unity of Invention is lacking. The lack of unity determination is still deemed proper and is therefore made FINAL.

2. **Claims withdrawn** :

Claims 1-8, 11-13 & 15-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed as per response filed November 29, 2004.

3. Claims 9, 10 & 14 are under consideration in this examination.

4. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on September 7, 1999.

5. ***Specification***

(a) The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors [or missing SEQ ID Nos.] of which applicant may become aware in the specification.

(b) ***Sequence Rules (Reminder)***

The instant specification on pages 17-19, present nucleotide or amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825, every disclosed amino acid sequence of four or more residues or 10 or more nucleotides must be identified by a SEQ ID NO. The amino acid sequences presented do not have SEQ ID NOs. In order to comply with the sequence

rules Applicants must identify these sequences by providing SEQ ID NO :, and where required provide a new version of the sequence listing and disk.

Applicant must submit a CRF copy and paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. j 1.821(e) or 1.821(9 or 1.821(g) or 1 .825(d), as well as an amendment directing its entry into the specification.

In case these sequences are already a part of the sequence listing, Applicants may simply amend their specification by inserting the appropriate SEQ ID NO:? at the end of each of these sequences.

New Sequence Rules

Since the effective filing date after July 1, 1998, Applicants should follow the New Rule Format and submit a new Sequence Listing (both in electronic and paper format). Compliance according to the requirements of 37 CFR 1.821 through 1.825 is required.

6. ***Claim Objections***

(a) Claims 9, 10 & 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 9 & 10, directly or indirectly depend upon non-elected claim 1. Claim 14 depend upon claim 12. Both claims 1 & 12 are non-elected claims. Amending the claims to place the claims in proper dependent form will overcome this objection.

(b) The following language is suggested during redrafting or amending claims: These are examples to highlight the examiners point of view and the purpose is to aid the Applicants in improving the quality of any issuing patent.

Claim 9 – A method of screening herbicidally active compound, which inhibit the activity of plant dihydroorotase.....using the DNA

sequence of claim 1 (which may be redundant, because the claim 1 is a non-elected claim).

Claim 10 – 'high-throughput screening (HTS) assay'.

Claim 14 – would require redrafting to overhaul the language, and would be best left to the Applicants' representative.

7. ***35 U.S.C. § 112, first paragraph (Written Description)***

Claims 9, 10 & 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 9, 10 & 14 are directed to a method for finding herbicidal active substances which inhibit the activity of a plant dihydroorotase, comprising producing dihydroorotase using the DNA sequence of claim 1 [or SEQ ID NO: 1] or a DNA sequence having at least 40% homology to SEQ ID NO: 1 and which encodes a protein having the biological activity of a dihydroorotase in the presence of a test compound.

The specification, however, only provides a single representative species of dihydroorotase from *Solanum tuberosum* [or SEQ ID NO: 2] for use in the method of screening for herbicidally active test compounds, wherein the inhibition of the dihydroorotase activity is taken as a measure of the effectiveness of the test compounds. The specification does not contain any disclosure or description of the structure and function of all DNA sequences that are 40% identical to SEQ ID NO: 1, or wherein such a DNA would likely encode polypeptide(s) having dihydroorotase activity. Dihydroorotase are a class of enzyme that catalyze the elimination of water from carbamoyl aspartate to form dihydroorotate. In plants, dihydroorotase exists as a separate enzyme; and is described to occur as a component of polyfunctional polypeptide or multi-enzyme complex in eukaryotes or yeast (see specification, pages 1-2).

However, the existence of the enzyme separately or as a complex does not demonstrate that an enzyme is suitable as a herbicide target, nor examples exits in the specification that describe and show that inhibiting the dihydroorotase will result in killing or controlling the plant growth, as would be expected of a herbicide. The specification also fails to describe any test compound(s) that has been used in order to inhibit or effect the dihydroorotase activity.

The genus of polynucleotides (60% modification of SEQ ID NO: 1) that comprise these DNA molecules and used in the method is a large variable genus with the potentiality of encoding many different proteins with no function, or polypeptides with no associated regulatory or biochemical function. Therefore, many functionally unrelated DNA or polypeptide molecules are encompassed within the scope of these claims, including partial DNA sequences and/or encoding polypeptide fragments. The specification discloses one species of the polypeptide [SEQ ID No. 2] and one species of the encoding polynucleotide [SEQ ID No. 1) of the claimed genus, which has not been disclosed to be representative of the larger genus claimed, and is therefore insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus of methods employing polynucleotides having 40% similarity and using these sequences in the preparation of vector, host cell and for making the polypeptide recombinantly. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. ***Claim Rejections - 35 USC § 112, first paragraph (Enablement)***

Claims 9-10 & 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method (or process) for finding herbicidal active substances by inhibiting the activity of a plant dihydroorotase, comprising producing dihydroorotase recombinantly using the

DNA sequence of SEQ ID NO: 1, does not reasonably provide enablement for using any DNA sequence having at least 40% homology to SEQ ID NO: 1 and which encodes a protein having the biological activity of a dihydroorotase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 9-10 & 14 are so broad as to encompass a method of identifying an inhibitor of any dihydroorotase, which is encoded by a DNA having at least 40% identity to SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of dihydroorotase broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence of SEQ ID NO: 1 and encoded amino acid sequence of dihydroorotase of SEQ ID NO : 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any dihydroorotase by modifying the DNA to have a homology of at least 40% to SEQ ID NO: 1, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting dihydroorotase activity; (B) the general tolerance of dihydroorotase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any dihydroorotase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including dihydroorotase with an enormous number of amino acid modifications of the of SEQ ID NO: 2 [as a result of modifying the DNA]. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of dihydroorotase(s) having the desired biological characteristics, and further use in the method for identifying herbicidal compounds is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9, line 6, recites 'biological activity of dihydroorotase'. The claim is indefinite because it is unclear what 'biological activity' is and the specification does not provide a basis for this recitation, which may include enzymatic or immunogenic activities. The most relevant to Applicants' method would be 'enzymatic'. Therefore replacing 'biological activity' with 'enzymatic activity' is suggested to overcome this rejection

10. Claims 9-10 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: claim 9 – measuring the plant dihydroorotase in the presence and absence of a test compound....

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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